

**AMENDMENT AND RESPONSE TO OFFICE ACTION**

**Amendment**

**In the Claims**

1. (currently amended) A composition comprising a matrix and a bidomain protein or peptide having an amino acid sequence that comprises a transglutaminase substrate domain and a ~~bioactive~~ polypeptide growth factor, wherein the protein or peptide is covalently bound to the matrix by the transglutaminase substrate domain.

2. (original) The composition of claim 1 wherein the matrix comprises fibrin.

3. (original) The composition of claim 2 wherein the transglutaminase substrate domain is a Factor XIIIa substrate domain.

4. (original) The composition of claim 3 wherein the Factor XIIIa substrate domain comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, and SEQ ID NO: 15, and combinations and bioactive fragments thereof.

5. (original) The composition of claim 3 wherein the Factor XIIIa substrate domain comprises an amino acid sequence of SEQ ID NO: 15.

Claim 6. (canceled)

7. (currently amended) The composition of claim 1 wherein the ~~bioactive~~ growth factor comprises an amino acid sequence selected from the group consisting of ~~SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6,~~ TGF- $\beta$ 1, BMP 2, VEGF<sub>121</sub>, PDGF AB, PTH, L11g6, and combinations and bioactive fragments thereof.

AMENDMENT AND RESPONSE TO OFFICE ACTION

Claim 8. (canceled)

9. (currently amended) The composition of claim 8 1 wherein the ~~bioactive-growth~~ factor is selected from the group consisting of VEGF, a growth factor from the TGF- $\beta$  superfamily, PDGF, ~~growth-hormone~~, IGF, and ephrin.

10. (previously presented) A method of attaching a ~~bioactive~~ polypeptide growth factor to a matrix, comprising

producing a ~~biomain~~ bidomain peptide or protein comprising a ~~bioactive~~ growth factor and a transglutaminase substrate domain; and

exposing the matrix to a transglutaminase to covalently couple the bidomain peptide or protein to the matrix and crosslink the matrix.

11. (original) The method of claim 10 wherein the matrix comprises fibrin.

12. (previously presented) The method of claim 10 wherein the transglutaminase substrate domain is a Factor XIIIa substrate domain and the transglutaminase is Factor XIIIa.

13. (previously presented) The method of claim 12 wherein the Factor XIIIa substrate comprises an amino acid sequence is selected from the group consisting of SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, and SEQ ID NO: 15, and a combination or bioactive peptide fragment thereof.

14. (previously presented) The method of claim 13 wherein the Factor XIIIa substrate comprises an amino acid sequence of SEQ ID NO: 15.

Claim 15. (canceled)

**AMENDMENT AND RESPONSE TO OFFICE ACTION**

16. (currently amended) The method of claim 10 wherein the bioactive growth factor is selected from the group consisting of VEGF, growth factors from the TGF- $\beta$  superfamily, PDGF, ~~growth hormone~~, IGF, and ephrin.

17. (currently amended) The method of claim 10 wherein the bioactive growth factor contains an acid sequence selected from the group consisting of ~~SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6~~, TGF- $\beta$ 1, BMP 2, VEGF<sub>121</sub>, PDGF AB, L11g6, and PTH, and a combination or bioactive peptide fragment thereof.

18. (currently amended) A bidomain protein or peptide comprising a transglutaminase substrate domain and a bioactive polypeptide growth factor.

19. (previously presented) The bidomain protein or peptide of claim 18 wherein the protein or peptide is a recombinant or synthetic protein or peptide.

20. (previously presented) The bidomain protein or peptide of claim 18 wherein the transglutaminase substrate domain is a Factor XIIIa substrate domain.

21. (previously presented) The bidomain protein or peptide of claim 20 wherein the Factor XIIIa substrate domain comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, and SEQ ID NO: 15, and combinations and bioactive fragments thereof.

22. (previously presented) The bidomain protein or peptide of claim 21 wherein the Factor XIIIa substrate domain comprises an amino acid sequence of SEQ ID NO: 15.

Claims 23-25. (canceled) .

**AMENDMENT AND RESPONSE TO OFFICE ACTION**

26. (currently amended) The bidomain protein or peptide of claim ~~25~~ 18 wherein the ~~bioactive-growth~~ factor is selected from the group consisting of VEGF, a growth factor from the TGF- $\beta$  superfamily, PDGF, ~~growth hormone~~, IGF, and ephrin.

27. (currently amended) The bidomain protein or peptide of claim 26 wherein the growth factor is selected from the group consisting of TGF- $\beta$ 1, VEGF<sub>121</sub>, PDGF AB, BMP 2, and L1lg6.

28. (currently amended) A matrix material for forming a gel comprising

(i) a bidomain protein or peptide comprising a transglutaminase domain and a ~~bioactive~~ polypeptide growth factor,

(ii) fibrinogen,

(iii) factor XIIIa, and

(iv) thrombin.

29. (previously presented) The matrix material of claim 28 wherein the transglutaminase substrate domain is a Factor XIIIa substrate domain.

30. (previously presented) The matrix material of claim 29 wherein the Factor XIIIa substrate domain comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, and SEQ ID NO: 15, and combinations and bioactive fragments thereof.

Claims 31-33. (canceled)

**AMENDMENT AND RESPONSE TO OFFICE ACTION**

34. (currently amended) The matrix material of claim ~~33~~ 28 wherein the ~~bioactive~~ growth factor is selected from the group consisting of VEGF, a growth factor from the TGF- $\beta$  superfamily, PDGF, ~~growth hormone~~, IGF, and ephrin.

35. (previously presented) The matrix material of claim 34 wherein the growth factor is selected from the group consisting of TGF- $\beta$ 1, VEGF<sub>121</sub>, PDGF AB, BMP 2, and L1Ig6.